THE INHERITABILITY OF PTSD: IDENTIFYING THE VULNERABLE

Suffering from post-traumatic stress disorder (PTSD) can be a challenge to raising emotionally-healthy children. Indeed, research has shown that children of parents with PTSD are themselves more susceptible to the condition. Now, the laboratory of Michael Meaney, PhD, at McGill University is starting to explain why.

Dr. Meaney specializes in the study of epigenetics, or changes in genetic expression that occur as a result of environmental influence and which may be inherited by the next generation. He has joined forces with Dr. Rachel Yehuda, from the Icahn School of Medicine at Mount Sinai, who has shown that children of Holocaust survivors are more vulnerable to PTSD and are more likely to have an endocrine "signature" characterized by low production of cortisol. "Cortisol can be protective against PTSD," says Dr. Meaney, "particularly in [those] who live in stressful circumstances."

COMBINING EXPERTISE

Could epigenetics play a role in this intergenerational association of parental PTSD with PTSD-related vulnerability in offspring? To find out, Dr. Meaney and colleagues identified 80 adults with at least one parent who was a Holocaust survivor and 15 adults of similar background whose parents were not in the Holocaust and did not have PTSD. They compared these two groups with respect to multiple psychological and biological factors.

Participants whose fathers, but not mothers, had PTSD (whether or not they were Holocaust survivors) had evidence of an epigenetic change consisting of higher methylation on the NR3C1 gene, which encodes for the glucocorticoid receptor. In contrast, those in whom both parents had PTSD had reduced methylation of this same gene. The investigators also demonstrated that increased methylation silences the activity of the gene and is associated with reduced cortisol suppression during a cortisol suppression test.

Similarly, the presence of symptoms of psychological distress in the subjects differed depending on whether their mother or father had PTSD. Those whose mothers only had PTSD were most likely to suffer from psychological scars, low perceived emotional health, depressive symptoms and anxiety. Those whose fathers only had PTSD also had some signs of psychological scars and anxiety, but they were more likely to suffer from problems associated with childhood trauma, such as sensitivity to stress and varieties of insecure attachment. If both parents had PTSD, offspring suffered the whole gamut of symptoms, but remarkably, their NR3C1 gene methylation was similar to those who had parents without PTSD.

PUTTING IT TOGETHER

Why the gender of the parent with PTSD is so significant remains unclear, but it is increasingly certain that children of people with PTSD are vulnerable at the level of biology and symptomatology. This work raises the hope that one day laboratory testing can be used to identify the most vulnerable people among at-risk populations using such biological markers as gene methylation much in the way blood tests are used today to help predict heart attack risk.

John O'Neil, MD, an expert in post-traumatic and dissociative disorders at St Mary's Hospital Center calls this "a marvelous example of where research needs to go… If you could match epigenetic changes to the resultant hormonal differences in children, then you would presumably be able to identify those that would be more susceptible to developing subsequent PTSD. Identifying whether these epigenetic changes are transmitted in the germline would be of enormous scientific interest, but in either case, since epigenetic changes are environmentally induced, in whichever generation, psychosocial interventions would remain crucial in treatment."

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Ref.: Yehuda R, Daskalakis NP, Lehrner A, Desarnaud F, Bader HN, Makotkine I, Flory JD, Bierer LM, Meaney MJ. Influences of maternal and paternal PTSD on epigenetic regulation of the glucocorticoid receptor gene in Holocaust survivor offspring. *American Journal of Psychiatry* 2014;171(8):872-880. doi:10.1176/appi.ajp.2014.13121571.